(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau





(43) International Publication Date 24 December 2003 (24.12.2003)

PCT

(10) International Publication Number WO 03/106381 A2

(51) International Patent Classification7:

C07C

(21) International Application Number: PCT/US03/18262

(22) International Filing Date: 11 June 2003 (11.06.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/388,326

12 June 2002 (12.06.2002) US

(71) Applicant (for all designated States except US): EX-ELIXIS, INC. [US/US]; P.O. Box 511, 170 Harbor Way, South San Francisco, CA 94083-0511 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): BANNEN, Lynne, Canne [US/US]; 801 St. Lawrence Drive, Pacifica, CA 94044 (US). CO, Erick, W. [US/US]; 921 Salt Court, Redwood City, CA 94065 (US). JAMMALAMADAKA, Vasu [US/US]; 2806 Maria Street, Pleasanton, CA 94588 (US). NUSS, John, M. [US/US]; 16 Woodranch Circle, Danville, CA 94506 (US). KIM, Moon, Hwan [US/US]; 1128 Oregon Avenue, Palo Alto, CA 94303 (US). LE, Donna, Tra [US/US]; 2591 Canary Palm Court, San Jose, CA 95133 (US). LEW, Amy [US/US]; 2977 S. Norfolk St.#209, San Mateo, CA 94403 (US). MAC, Morrison, B. [US/US]; 2567 30th Avenue, San Francisco, CA 94116 (US). MAMO, Shumeye [US/US]; 3030 School Street,

Oakland, CA 94602 (US). WEN, Zhaoyang [US/US]; 357 Baltimore Way, San Francisco, CA 94112 (US). XU, Wei [US/US]; 327 Glasgow Circle, Danville, CA 94526 (US).

- (74) Agents: GRIEDEL, Brian et al.; Exelixis, Inc., P.O. Box 511, 170 Harbor Way, South San Francisco, CA 94083-0511 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

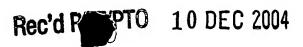
 without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: HUMAN ADAM-10 INHIBITORS

OF ON Tina

(57) Abstract: The present invention provides compounds useful for inhibiting the ADAM-10 protein, with selectivity versus MMP-1. Such compounds are useful in the *in vitro* study of the role of ADAM-10 (and its inhibition) in biological processes. The present invention also comprises pharmaceutical compositions comprising one or more ADAM-10 inhibitors according to the invention in combination with a pharmaceutically acceptable carrier. Such compositions are useful for the treatment of cancer, arthritis, and diseases related to angiogenesis. Correspondingly, the invention also comprises methods of treating forms of cancer, arthritis, and diseases related to angiogenesis in which ADAM-10 plays a critical role.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/18262

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A61K 31/495, 31/496, 31/5377; C07D 241/04, 401/06, 401/12, 403/06, 403/12, 413/06, 413/12. US CL : 514/235.8, 252.11, 253.01, 253.05, 253.13, 254.01, 255.01; 544/121,357,360, 365, 372, 383. According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S.: 514/235.8, 252.11, 253.01, 253.05, 253.13, 254.01, 255.01; 544/121,357,360, 365, 372, 383.						
Documentation sea	arched other than minimum documentation to the	extent that	such documents are included	in the fields searched		
	se consulted during the international search (name RUCTURE SEARCH AND CASREACT SEARCH		ase and, where practicable, so	earch terms used)		
C. DOCUMEN	NTS CONSIDERED TO BE RELEVANT					
Category *	Citation of document, with indication, where ap	propriate, c	of the relevant passages	Relevant to claim No.		
X 6, 8 US 6 1-3,	US 5,753,653 A (BENDER et al.) 19 May 1998 (19.05.1998), see especially columns 4-6, 8 and 12 and examples 1-9 in columns 25-35. US 6,333,324 B1 (NEYA et al.) 25 December 2001 (25.12.2001), see especially columns 1-3, 7 and examples 19,25,27-30 in columns 32,37,38. US 6,664,291 B2 16 December 2003 (16.12.2003), see column 38, lines 5-12.			1-3,6-9,11- 13,15,16,51-53 and 1-3,10-12,15-16,29- 33,51-53 54-63		
Further docu	ments are listed in the continuation of Box C.		See patent family annex.	41		
"A" document defining be of particular a	categories of cited documents: ing the general state of the art which is not considered to relevance on or patent published on or after the international filing	"X"	later document published after the in priority date and not in conflict with understand the principle or theory ut document of particular relevance; the considered novel or cannot be considered novel or cannot to	the application but cited to deriying the invention cannot be lered to involve an inventive		
"L" document which	n may throw doubts on priority claim(s) or which is cited publication date of another citation or other special reason		document of particular relevance; the considered to involve an inventive st combined with one or more other su combination being obvious to a persu	e claimed invention cannot be ep when the document is th documents, such		
"O" document referri	nent referring to an oral disclosure, use, exhibition or other means		document member of the same patent	family		
	shed prior to the international filing date but later than the	"&"				
Date of the actual	completion of the international search	Date of m	ailing of the international sea	rch report		
17 January 2004 (1	17.01.2004)	2 % FEB 2004 ,				
	address of the ISA/US	Authorize	d officer //	1.		
Mail Stop Commissio P.O. Box	PCT, Attn: ISA/US ioner for Patents	Emily Bo	ernhardt (allery for		
Facsimile No. (703			<i>i</i>			
orm PCT/ISA/210	(second sheet) (July 1998)		-	7		





INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/18262

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)					
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:					
Claim Nos.: because they relate to subject matter not required to be searched by this Authority, namely:					
2. Claim Nos.: 1-13,15-27,29-33,35-40,51-53, and 64-66 (all in part) because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically: Please See Continuation Sheet					
3. Claim Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).					
Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)					
This International Searching Authority found multiple inventions in this international application, as follows:					
1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.					
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.					
As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:					
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:					
Remark on Protest The additional search fees were accompanied by the applicant's protest.					
No protest accompanied the payment of additional search fees.					

Form PCT/ISA/210 (continuation of first sheet(1)) (July 1998)





INTERNATIONAL SEARCH REPORT

PCT/US03/18262	-

Continuation of Box I Reason 2:

The claims relate to an extremely large number of permutations based on the scope of variables claimed as generically set forth in the claims which are not all adequately supported in the description within the meaning of PCT Article 6. The claims have been searched based on the U.S. classification of the working examples in the description and particularly claimed in claims 14,28,34,41,54-63 and 67-69.

It has been noted that there are no claims numbered 42-50. On page 90 after claim 41 follows claim 51,etc.